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July 7, 1989

FILE: UTSK:097

Commissioner of Patents
and Trademarks
Washington, D.C. 20231

Re: SN 07/313,911 "Method and Apparatus for Direct Measurement of Hemoglobin Species in Whole Blood"--Steinke, et al. (UTHSC/SA:085)

Sir:

Enclosed for filing in the above-referenced patent application is an Information Disclosure Statement, PTO-Form 1449 and 36 references.

Please stamp and return the enclosed postcard evidencing receipt of these materials.

Respectfully submitted,

David D. Bahler
Reg. No. 30,932

DDB:bp
Enclosures
cc: Dr. A. P. Shepherd (w/enclosures)
John M. Steinke (w/enclosures)
Dudley R. Dobie, Jr., Esq. (w/enclosures)
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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: §
A. P. Shepherd and §
John M. Steinke §
§ Examiner: Unknown
Serial No. 07/313,911 §
§ Group Art Unit: 255
Filed: February 23, 1989 §
§ Atty. Dkt: UTSK:097/BAH
For: METHOD AND APPARATUS FOR §
DIRECT MEASUREMENT OF §
HEMOGLOBIN SPECIES IN §
WHOLE BLOOD §

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner of Patents and Trademarks, Washington, D.C. 20231, on July 7, 1989
(Date of Deposit)
David D. Bahler
Name of applicant, assignee, or Registered Representative
Signature
July 7, 1989
Date of Signature

INFORMATION DISCLOSURE STATEMENT

Commissioner of Patents
and Trademarks
Washington, D. C. 20231

Sir:

In compliance with the duty of disclosure under 37 C.F.R. § 1.56, it is respectfully requested that this Information Disclosure Statement be entered and the documents listed on attached Form PTO-1449 be considered by the Examiner and made of record. Copies of the listed documents are enclosed for convenience of the Examiner.

In accordance with 37 C.F.R §1.97(b), this Information Disclosure Statement is not to be construed as a representation that a search has been made or that no other possibly material information as defined in 37 C.F.R §1.56(a) exists.

The comments contained in this Information Disclosure Statement are believed to constitute a concise explanation of the relevance of each listed document to the invention claimed in the

present application. 37 C.F.R §1.98(a). These comments, however, are not intended to take the place of the Examiner's complete consideration of each listed reference.

Patent 3,799,672 relates to an oximeter for measuring the percentage of hemoglobin saturated with oxygen. The specification indicates that both infrared and red light emitting diodes (LEDs) are utilized. A ratio of the two optical signals are used in computing blood oxygen saturation. The specification further indicates that hematocrit error is reduced when the optical paths from the red and infrared signals to the photodetector are as identical as possible. To ensure equal optical paths, holes are provided for the light emitting diodes which are perpendicular to the blood-filled cuvette and equally spaced from the photodetector.

Patent 4,134,678 relates to an automatic blood analysis apparatus that appears capable of analyzing both hemoglobin concentration and percentage of hemoglobin saturated with oxygen. At column 3, line 29-39, the authors indicate that four different wavelength spectral lines are used to measure the various hemoglobin species, and the total hemoglobin is found by adding the four species concentrations. The specification further indicate that the apparatus can analyze either diluted or whole, undiluted blood. However, if whole, undiluted blood is used a series of pump-cages and coils are necessary for hemolyzing the blood for measurement. (Col. 6, lines 19- Col. 7, lines 8.)

Patent 3,692,410 relates to a measuring device for determining hemoglobin content and hematocrit value of blood samples by means of optical glass prisms permitting the light transillimination of undiluted blood sample. (Col. 1, lines 5-11.) The specification further discloses dual prisms in contact with a blood sample wherein a light pencil emitted by a light source passes through the first prisms where it is deflected by 90°, then it passes through a blood layer where it is received by the second prisms where it is again deflected and is finally received on a photoelectric sensor. (Col. 2, lines 21-26.) Accordingly, the hemoglobin content of the undiluted blood sample is calculated from the spectral light transmissivity and electrical conductivity between the electrodes.

Patent 3,638,640 discloses an oximeter and a method for determining the oxygen saturation in blood. The oximeter apparatus directs radiation from three or more wavelengths into skin tissue or a blood-confining container. Contained within the oximeter is circuitry for combining the detector outputs in a predetermined manner to provide logarithmic output of the detector responses wherein such responses are linearly combined to yield an indication of the oxygen saturation as the ratio of the concentration of oxyhemoglobin to the concentration of total hemoglobin present. (Col. 2, lines 11-114.)

Patent 4,651,741 relates to a method of measuring blood oxygen saturation by fiber optical means. The specification indicates that a ratio of both red and infrared light is used in

calculating the oxyhemoglobin saturation value. As the red to infrared intensity ratio, I, and the hematocrit values A, B and C change, so must the oxyhemaglobin saturation measurement value.

Patent 4,013,417 relates to a apparatus for simultaneously measuring total hemoglobin, percent oxyhemoglobin and percent of various hemoglobin species using an oxygen electrode in a dual wavelength optical system for measuring PO_2 and absorbants. The specification states that in order to obtain a reasonable value of absorbance in an ordinary 1.0 cm light path cuvette, normal blood must be diluted 100 times. (Col. 2, lines 62-64.)

Patent 3,972,614 relates to a method and apparatus for measuring one or more data of blood samples, such as oxygen saturation, contents of hemoglobin and constituents of blood samples. The blood samples are hemolyzed by imparting ultrasonic waves. For purposes of determining oxygen saturation and/or hemoglobin concentration, the apparatus comprises a photometric measuring device arranged at the hemolyzing conduit section in order to avoid movement of the blood sample within said conduit after hemolyzation prior to measurement thereof. (Col. 2, lines 16-25.)

Patent 4,605,305 relates to a laser nephelometer for sensing antigens and antibodies suspended in a capillary tube. The capillary tube has an inner diameter between 0.3 and 1.3 mm. (Col. 3, lines 13-14.)

Patent 4,324,556 relates to a portable spectrophotometric apparatus for measuring the percentage of carboxyhemoglobin

(COHb) in blood. The apparatus comprises wavelength selection filters for testing a reference sample having a hemolizing agent and a treated blood sample for determining relative absorbance values of the two samples at wavelengths of 420 and 432 nm.

Patent 4,565,448 relates to a particle counting apparatus for counting particles entrained in a fluid medium flow. The apparatus has a cyclindrical board for accommodating a cuvette extending therethrough, the axis of the board being parallel to the direction of particle flow through the cuvette.

Patent 4,453,266 relates to a method of an apparatus for measuring and reporting size information about red blood cells and particularly mean cell volume of red blood cells in a blood specimen and for generating signals representative of the hemoglobin content or mass of the cells. (Col. 1, lines 8-16.)

Patent 4,357,105 relates to a spectrophotometer instrument, and is particularly dedicated to hemoglobin determination employing an LED light source with a peak output wavelength of about 553 nm.

Patent 3,994,585 relates to an opto-electrical measuring apparatus for determining the relative hemoglobin content of an illuminated hemoglobin solution. The illuminated hemoglobin solution is arranged in a path of light between a light source and a photoelectric transducer, wherein hemoglobin content is evaluated by light absorption over a predetermined wavelength range of 500 to 600 nm. (Col. 1, lines 9-15 and col. 2, lines 3-20.)

Patent 4,003,662 relates to a portable photometer for measuring the proportion of hemoglobin in human blood. (Col. 1, lines 17-25.) The specification discloses a cuvette, a color filter and focusing lens placed within the path of the light beam, and a wedge filter moveably arranged in the path of the light beam. A photographic element receives the light from the light beam and produces an electrical voltage corresponding to the intensity of the light beam. (Col. 2, lines 48-52.) The adjustment of the wedge filter is related to the light permeability of liquid in a cuvette and is indicated by a graduated scale. (Col. 4, lines 17-21.)

Patent 4,444,498 relates to an oximeter device which includes: a specially-designed cuvette through which blood flows as it is being monitored; sensors which alternatively illuminate and read reflected light signals obtained from blood passing through the curvette; and, a circuit which uses optical feedback to match the light output of two different wavelength light sources and to set the absolute level of light reflected back from the blood to the sensor to compensate for wide variations of hematocrit levels by assuring uniform depth of penetration of light into the blood sample. (Col. 1, line 66 through col. 2, line 46.) The curvette must be specially designed to provide optimum light penetration, minimum stray surface reflection, and good dynamic signal levels over wide hematocrit range changes.

Patent 4,243,883 relates to a system for continuously monitoring and/or controlling blood hematocrit levels. Referring

to Fig. 2, and optically transparent lumen 22, that is generally circular in cross section at the entrance and the exit of housing 30 but is generally square in cross section in the middle between a light source and the detector, is inserted in the main blood flow loop and disposed between an infrared light source 24 and a phototransistor detector 26. The components of the detector are stated to be selected so that the amount of light striking the detector surface is directly related to the hemoglobin density in the optical path. (Col. 3, lines 3-11.) The hematocrit level appears to be related empirically as linear function of light intensity. (See, Fig. 4.) The linear response is achieved by the electrical components of the device. (Col. 4, lines 36-37.)

Patent 3,296,922 relates to an apparatus for evaluating the oxygen saturation of blood. The device uses a dual beam principle wherein a beam of light of one wave length (805 millimicrons) is compared with a beam of another wave length (660 millimicrons), the beams being diffusely reflected with a blood sample. (Col. 1, lines 62-69.) Oxygen saturation is determined by attenuating the 660 millimicron beam in amounts sufficient to match the intensity of the 805 millimicron beam reflected from the same blood so as to determine the difference in intensities of the two beams. (Col. 2, lines 10-26.) The specification further indicates that the use of two wavelength renders the result independent of hematocrit within wide limits. (Col. 12, lines 46-48.)

Patent 4,502,786 relates to a system for automatically determining the amount of hemoglobin species in a first blood sample relative to the total hemoglobin of a second blood sample. (Col. 1, lines 16-19.) A beam splitter means is provided to reflect parallel rays of light from a light source into two opposite directions so that the same source of light may be utilized to simultaneously determine the concentration of the first and second solutions. (Col. 5, lines 33-38.) The specification indicates that during operation, one sample is prepared containing the hemoglobin species of interest, and a second sample is prepared containing the remaining hemoglobins. Each sample is then separately placed in the device for simultaneously measuring the transmittance of the two samples. (Col. 2, lines 32-56.)

Patent 3,764,267 relates to an apparatus for measuring the hemoglobin content of whole blood. The specification indicates that whole blood contained in a calibrated capillary sample tube must be mixed with a continuous uniform stream of reagent liquid from the pump through one pump discharge cycle. (Col. 2, lines 8-13.) Once a proper mixture is obtained, a light sensing means is provided to measure the diluted hemoglobin sample.

Patent 4,770,708 relates to a probe apparatus for use with an optical oximeter wherein light of two different wavelengths is passed through any human or animal body pulsatile tissue bed thereby allowing indication of oxygen saturation. (Col. 4, lines 23-29.) Light emitted from the two LEDs enters the pulsatile

tissue bed, and after being subjected to diffusion and scattering, is measured by a sensor. (Col. 5, lines 42-47.)

Patent 2,812,707 relates to an apparatus for improved reading of hematocrit tubes.

Patent 4,240,749 relates to a test vessel designed for housing a capillary tube used for taking up a sample to be measured with a photometer.

Patent 4,308,029 relates to a method for deoxygenating a blood sample in a capillary tube for use therein.

Reissue patent 30,007 relates to a method and apparatus for determining the hematocrit of blood samples by using the electrical conducting properties of whole blood.

Patent 4,301,412 also relates to a system for measuring conductivity of body fluids and, in particular, to a system for automatically measuring hematocrit and giving an approximation of hemoglobin. The specification illustrates that the apparatus obtains hematocrit measurements from the electrical conductivity of the blood sample.

Patent 3,527,542 relates to a cuvette apparatus adapted to support disposable, flow-through cuvettes in proper orientation with respect to the photometric analyzers forming part of cardiac output apparatus.

Patent 2,878,715 relates to an apparatus for measuring blood plasma prothrombin time determinations wherein a spectro photometer and photo electric detection is used. The apparatus comprises an adapter having an outer casing of generally tubular

form preferably made of machined aluminum designed to accommodate a 10 mm culture tube or cuvette.

Patent 4,303,887 also relates to the measurement of electrical conductivity of whole blood.

Patent 4,057,394 relates to a matrix test device wherein a test sample of blood is contacted with the matrix and the light reflectance therefrom is measured as an indicator of the quantitative amount of hemoglobin present in the blood sample. (Col. 2, lines 19-24.) The matrix, having an index of refraction significantly different from the blood sample, is used as a medium of permeability of an applied blood sample.

Document AA (Kiel and Shepherd) relates to a system for measuring the percentage of oxyhemoglobin in the flow of whole blood. This system comprises a personal computer analog-to-digital converter, a photo detector circuit having two approximate wavelengths, and a short program in BASIC. The authors describe the basic method of oxyhemoglobin measurement comprising optical absorbance/light scattering techniques. Necessary hardware and software design is further described.

Document AB (Steinke and Shepherd) illustrates total scattering effects as a function of wavelength in oxygenation. Furthermore, the authors indicate that the relationship between total scattering effects and percent oxygenation was approximately linear, and that scattering effects in the red and infrared range do not detract from the linearity of whole blood oximeters.

Document AC (Anderson and Sekelja) relates to the light/scattering properties that occurs in undiluted blood. The abstract indicates that there is parabolic relationship between light scattering and red-cell concentration, and that the absorption of light within the erythrocyte is the same as in a hemoglobin solution.

Document AD (Kramer, et al.) relates to the measurement of oxygen saturation when red and infrared lights are transmitted in whole blood. The authors point out that for each erythrocyte concentration the relationship between oxygen saturation and the logirithm of light transmittance is a linear function. As stated in the summary, the theoretical assumption of Beer's Law does not apply to the determination of the oxygen saturation of whole blood from the transmittance of red and near-infrared light.

Document AE (Janssen) indicates that oxygen saturated blood can be determined by a photometric devices using whole blood. The author's analysis begins with the absorption and scattering properties of light in whole blood. The abstract further indicates that the diffusion theory under study can be applied to an oxymeter having a three dimensional design.

Document AF (Drabkin) relates to the crystallization of the hemoglobins and myoglobins of man and other species.

Document AG (Takatani, et al.) discloses a miniature reflection-type optical sensor for measurement of hemoglobin content and oxygen saturation of whole blood.

Document AH (Singh and Joseph) relates to a laser-based hematocrit measurement technique.

Applicant respectfully requests that the foregoing documents be made of record in the present case.

Respectfully submitted,

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